

## PATENT COOPERATION TREATY

PCT

NOTIFICATION CONCERNING  
AMENDMENTS OF THE CLAIMS(PCT Rule 62 and  
Administrative Instructions, Section 417)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark  
Office  
(Box PCT)  
Crystal Plaza 2  
Washington, DC 20231  
ETATS-UNIS D'AMERIQUE

in its capacity as International Preliminary Examining Authority

Date of mailing:

27 May 1997 (27.05.97)

International application No.:

PCT/US96/14250

International filing date:

28 August 1996 (28.08.96)

Applicant:

NEW YORK MEDICAL COLLEGE et al

The International Bureau hereby informs the International Preliminary Examining Authority that no amendments under Article 19 have been received by the International Bureau (Administrative Instructions, Section 417)

RECEIVED  
NOV 23 1997  
G.The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorised officer:

Martine Lee

Telephone No.: (41-22) 730.91.11

## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

MacWRIGHT, Robert, S.  
Skadden, Arps, Slate, Meagher &  
Flom  
919 Third Avenue  
New York, NY 10022  
ETATS-UNIS D'AMERIQUE

SEP 23 1997

Date of mailing (day/month/year) 12 June 1997 (12.06.97)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 1075PCT	
International application No. PCT/US96/14250	International filing date (day/month/year) 28 August 1996 (28.08.96)

## 1. The following indications appeared on record concerning:

☒ the applicant ☐ the inventor ☐ the agent ☐ the common representative

Name and Address NEW YORK MEDICAL COLLEGE Valhalla, NY 10595 United States of America	State of Nationality US	State of Residence US
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

Name and Address NEW YORK MEDICAL COLLEGE Office of Research Administration Administration Building Room 202 Grasslands Avenue Valhalla, NY 10595 United States of America	State of Nationality	State of Residence
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

## 3. Further observations, if necessary:

## 4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned  
☐ the International Searching Authority ☒ the elected Offices concerned  
☒ the International Preliminary Examining Authority ☐ other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Martine Lee Telephone No.: (41-22) 338.83.38
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# PATENT COOPERATION TREATY

**PCT**

## NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

MacWRIGHT, Robert, S.  
Skadden, Arps, Slate, Meagher &  
Flom  
919 Third Avenue  
New York, NY 10022  
ETATS-UNIS D'AMERIQUE

<b>Date of mailing (day/month/year)</b> 12 June 1997 (12.06.97)	<b>IMPORTANT NOTIFICATION</b>
<b>Applicant's or agent's file reference</b> 1075PCT	
<b>International application No.</b> PCT/US96/14250	<b>International filing date (day/month/year)</b> 28 August 1996 (28.08.96)

**1. The following indications appeared on record concerning:**

☒ the applicant      ☐ the inventor      ☐ the agent      ☐ the common representative

<b>Name and Address</b> NEW YORK MEDICAL COLLEGE Valhalla, NY 10595 United States of America	<b>State of Nationality</b> US	<b>State of Residence</b> US
	<b>Telephone No.</b>	
	<b>Facsimile No.</b>	
	<b>Teleprinter No.</b>	

**2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:**

☐ the person      ☐ the name      ☒ the address      ☐ the nationality      ☐ the residence

<b>Name and Address</b> NEW YORK MEDICAL COLLEGE Office of Research Administration Administration Building Room 202 Grasslands Avenue Valhalla, NY 10595 United States of America	<b>State of Nationality</b>	<b>State of Residence</b>
	<b>Telephone No.</b>	
	<b>Facsimile No.</b>	
	<b>Teleprinter No.</b>	

**3. Further observations, if necessary:**

**4. A copy of this notification has been sent to:**

☒ the receiving Office      ☐ the designated Offices concerned  
☐ the International Searching Authority      ☒ the elected Offices concerned  
☒ the International Preliminary Examining Authority      ☐ other:

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	<b>Authorized officer</b>  Martine Lee  Telephone No.: (41-22) 338.83.38
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## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark  
Office  
(Box PCT)  
Crystal Plaza 2  
Washington, DC 20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year)

27 May 1997 (27.05.97)

International application No.

PCT/US96/14250

Applicant's or agent's file reference

1075PCT

International filing date (day/month/year)

28 August 1996 (28.08.96)

Priority date (day/month/year)

30 August 1995 (30.08.95)

Applicant

DARZYNKIEWICZ, Zbigniew et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

26 March 1997 (26.03.97)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Martine Lee

Telephone No.: (41-22) 730.91.11

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: ROBERT S. MACWRIGHT  
SKADEN, ARPS, SLATE  
MEAGHER & FLOM  
919 THIRD AVENUE  
NEW YORK, NY 10022

## PCT

### NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference 1075PCT	Date of Mailing (day/month/year) <b>18 DEC 1996</b>
International application No. PCT/US96/14250	International filing date (day/month/year) 28 AUGUST 1996
Applicant NEW YORK MEDICAL COLLEGE	

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.  
**Filing of amendments and statement under Article 19:**  
 The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):  
**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.  
**Where?** Directly to the International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland  
 Facsimile No.: (41-22) 740.14.35  
**For more detailed instructions, see the notes on the accompanying sheet.**
2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.
3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
  - ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
  - ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.
4. **Further action(s):** The applicant is reminded of the following:
  - Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.
  - Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).
  - Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer: <i>DIANNE REES</i> <b>DIANNE REES</b> Telephone No. (703) 308-0196
Facsimile No. (703) 305-3230	

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 1075PCT	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US96/14250	International filing date (day/month/year) 28 AUGUST 1996	(Earliest) Priority Date (day/month/year) 30 AUGUST 1995
Applicant NEW YORK MEDICAL COLLEGE		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ Certain claims were found unsearchable (See Box I).
2. ☐ Unity of invention is lacking (See Box II).
3. ☐ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing
  - ☐ filed with the international application.
  - ☐ furnished by the applicant separately from the international application,
    - ☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
  - ☐ transcribed by this Authority.
4. With regard to the title,
  - ☒ the text is approved as submitted by the applicant.
  - ☐ the text has been established by this Authority to read as follows:
5. With regard to the abstract,
  - ☒ the text is approved as submitted by the applicant.
  - ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. The figure of the drawings to be published with the abstract is:  
Figure No. \_\_\_\_\_
  - ☐ as suggested by the applicant.
  - ☐ because the applicant failed to suggest a figure.
  - ☐ because this figure better characterizes the invention.☒ None of the figures.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US96/14250

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) : C12Q 1/68, 1/70; C12P 19/34; CO7H 21/04; CO7K 16/00

US CL : 435/6, 5, 91.1, 91.2; 536/24.3; 530/388.21

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 5, 91.1, 91.2; 536/24.3; 530/388.21

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JIRIKOWSKI, G.F. In situ hybridization of semithin Epon sections with BrdU labelled oligonucleotide probes.	1-4
-	Histochemistry. June 1990. Volume 94, Number 1, pages 187-190, especially page 188, column 2.	----
Y		5-20
X	JIRIKOWSKI, G.F. et al. Immunocytochemistry of 5-bromo-2' deoxyuridine labelled oligonucleotide probes: A novel technique for in situ hybridization. Histochemistry. Volume 91, Number 1, pages 51-53, especially page 51, column 2.	1-4
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Y		5-20
Y	US, 5,053,336 A (VANDERLAAN et al) 01 October 1991, see entire document.	1-20
Y	US, 4,851,331 A (VARY et al) 25 July 1989, column 10.	5-11



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	*T	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X*	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*E* earlier document published on or after the international filing date	*Y*	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*&*	document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means		
*P* document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

09 DECEMBER 1996

Date of mailing of the international search report

18 DEC 1996

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20541

Facsimile No. (703) 305-3230

Authorized officer

DIANNE REES

Telephone No. (703) 308-0196

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/14250

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, 4,780,406 A (DOLBEARE et al) 25 October 1988, see entire document.	12-20
Y,P	US, 5,500,432 A (NICOLAOU et al) 19 March 1996, see Figure 1.	12-20



**B. FIELDS SEARCHED**

Electronic data bases consulted (Name of data base and where practicable terms used):

APS, BIOSIS, BIOTECHABS, BIOBUSINESS, CANCERLIT, CABA, CAPLUS, DRUGU, EMBASE, MEDLINE, TOXLINE, TOXLIT, SCISEARCH, USPATFULL, WPIDS, JAPIO, IFIPAT

search terms: halogenated deoxyribonucleotides, brominated deoxyribonucleotides, BrdU, BrdUTP, BrdUMP, halogenated nucleosides, apoptosis, flow cytometry, end-labeling, end-labelling, TdT, or terminal deoxynucleotidyl transferase.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/14250

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC(6) : C12Q 1/68, 1/70; C12P 19/34; C07H 21/04; C07K 16/00 US CL : 435/6, 5, 91.1, 91.2; 536/24.3; 530/388.21 According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) U.S. : 435/6, 5, 91.1, 91.2; 536/24.3; 530/388.21 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Extra Sheet.		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	JIRIKOWSKI, G.F. In situ hybridization of semithin Epon sections with BrdU labelled oligonucleotide probes. Histochemistry. June 1990. Volume 94, Number 1, pages 187-190, especially page 188, column 2.	1-4 ---- 5-20
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Y	US, 5,053,336 A (VANDERLAAN et al) 01 October 1991, see entire document.	1-20
Y	US, 4,851,331 A (VARY et al) 25 July 1989, column 10.	5-11
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 09 DECEMBER 1996		Date of mailing of the international search report 18 DEC 1996
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230		Authorized officer DIANNE REES Telephone No. (703) 308-0196

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/14250

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, 4,780,406 A (DOLBEARE et al) 25 October 1988, see entire document.	12-20
Y,P	US, 5,500,432 A (NICOLAOU et al) 19 March 1996, see Figure 1.	12-20

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/14250

### B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

APS, BIOSIS, BIOTECHABS, BIOBUSINESS, CANCERLIT, CABA, CAPLUS, DRUGU, EMBASE, MEDLINE, TOXLINE, TOXLIT, SCISEARCH, USPATFULL, WPIDS, JAPIO, IFIPAT  
search terms: halogenated deoxyribonucleotides, brominated deoxyribonucleotides, BrdU, BrdUTP, BrdUMP, halogenated nucleosides, apoptosis, flow cytometry, end-labeling, end-labelling, TdT, or terminal deoxynuceotidyl transferase.